PERSPECTIVE



Barriers to global pharmacometrics: educational challenges and opportunities across the globe

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During the past three decades, pharmacometrics has developed considerably and gained recognition globally and across disciplines, causing the demand of well-trained pharmacometricians to outweigh the availability. Thus, high-quality and widespread education of pharmacometricians is key. A symposium and panel discussion titled "Training of the Next Generation of Pharmacometric

Talent Around the World" at the third World Conference on Pharmacometrics (WCoP2022, Cape Town) explored this issue and resulted in the perspective presented here.

Pharmacometrics is a complex and multidisciplinary scientific field with strong interplay between academia and industry. As a consequence, pharmacometrics education is associated with both opportunities and

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challenges,^{2,3} prompting unique initiatives and networks across the globe.⁴⁻⁶ Approximately 15 years after starting a number of educational initiatives,⁷⁻⁹ their impact needs to be discussed with respect to the initial purpose and how to move forward from them. Therefore, a symposium was held at WCoP2022, a hybrid event with approximately 300 participants worldwide, which aimed to share different perspectives on pharmacometric education and to obtain a global perspective.

THE SYMPOSIUM: INTERNATIONAL PERSPECTIVES AND AUDIENCE INPUT

The symposium consisted of six talks where international speakers with diverse backgrounds, all of which are actively training pharmacometric talents, presented their experiences and perspectives on the required skillsets of future pharmacometricians, education and training concepts, and related challenges and opportunities, followed by a panel discussion with contributions from the audience. The talks and discussion made clear that different challenges and opportunities for pharmacometrics training exist across the globe, with some being specific for certain localities and others being consistent worldwide, showing high intra- and interregional differences. A depiction of the main ones is provided in Figure 1 and more details, including the recordings of all talks, representing successful examples, can be found in the Supplementary Material. In the remainder of this perspective, we aim to synthesize the insights of the symposium into three clearly grouped challenges and opportunities which need tailored approaches: the movement of human capital, the multidisciplinary nature and the unbalanced spread of pharmacometrics across regions.

Challenges and opportunities related to the movement of human capital ("braindrain")

Pharmacometricians trained in low- and middle-income countries often move to the European Union or United States, leading to a brain-drain and difficulties in establishing not only larger teaching and training groups in these countries but also a stronger local pharmacometrics community ("geographic brain-drain"). The use of remote working opportunities should in theory allow a dampening of this geographic brain-drain, especially in an in silico field such as pharmacometrics. However, as echoed by the panelists during the symposium and the panel discussion (Supplementary Material), in practice this is not (yet) the case and both pharmaceutical companies and consulting companies hire mostly from EU, USA and Oceania or require working visas at these locations. Furthermore, academic centers, regardless of location, encounter increasing difficulty to attract and retain researchers at the post-doctoral, early to midcareer level and even senior faculty level. Not re-filling open positions as already observed presents a global threat eventually leading to fewer academic centers that offer opportunities for the next generation in the long-term. This in turn makes teaching and training activities and sustainability more challenging, leading to a loss of critical mass to sustain teaching ("academic

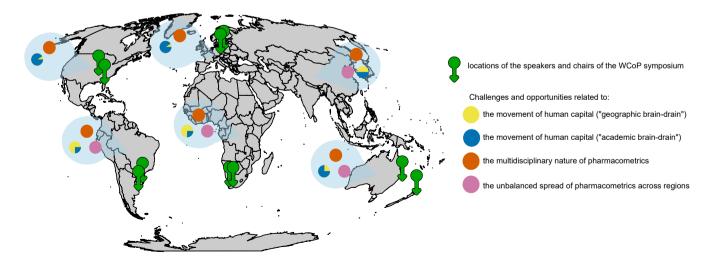
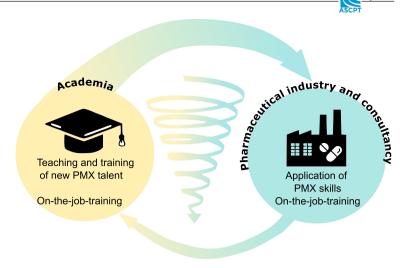


FIGURE 1 The local and global challenges for pharmacometrics training and education. Green dots with arrows represent locations of the speakers of the World Conference on Pharmacometrics symposium, and colored circles represent the different challenges and opportunities to tackle them, which are further discussed in the text. The ratio of academic to geographic movement of human capital is depicted semantically using two colors in the same circle.

FIGURE 2 Imbalanced flow of pharmacometricians between academia, and pharmaceutical industry and consultancy, leading to a possible decrease in newly trained pharmacometric talent.



brain-drain"; Figure 2). Both brain-drains especially the case in LMIC, where a critical mass of pharmacometricians is not always present. A minimum expression of a critical mass is needed to generate human resources and capabilities at a local level, and furthermore to connect the local community with the rest of the field globally. As long as this is not achieved, the above-described brain-drain will be the status quo in those countries, preventing the local communities to significantly supply the world with human resources. Therefore, aiming for trained pharmacometricians developing the discipline outside of Europe and US, e.g. by joint efforts such as Pharmacometrics Africa, RedIF and PAGANZ should be seen as part of the way forward. However, a stronger collaboration between academia and industry could be an opportunity for local development of pharmacometricians within an academic setting. Initiatives such as internships, industry mentors, on-site visits and projects using shared data (e.g., also from preclinical studies) are potential ways in which students and mid-level researchers can strive for a "best-of-two-worlds" approach. Academia and consulting companies are currently fostering this approach by "sharing" and offering part-time employees training and supervising opportunities. This might reduce the need to move away from their local or academic position. This stronger collaboration could also lead to increased mentoring support from industry in the form of e.g. industry mentors, expert knowledge sharing and providing guidance to students and early-career scientists. Indeed, sharing expertise back to academia is one of the essential points how industry partners can contribute towards moving forward from the status quo. Lastly, financial and logistic support for student scholarships, attendance of conferences, or fund academic-industry exchanges, especially from industry, for the training of the next generation of pharmacometrics talents might stimulate dedicated programs to stay active or grow capacity and attract talents to academic

positions, which might make a (part-time) academic career more attractive for scientists.

Challenges and opportunities related to pharmacometrics as a multidisciplinary field

Due to the multidisciplinary nature of pharmacometrics, there are two key challenges to exploring the potential of yet not identified next-generation talents: undergraduate students with the right skill set and mind-set need to be attracted background-specifically to the discipline and opportunities of pharmacometrics that are mostly new for them. Background-specific material could be developed to this end in a global effort. The curriculum of any academic training program should, especially at the beginning, acknowledge this diversity in backgrounds. Yet, all involved will quickly learn and see the diversity as an advantage. A critical aspect in developing the multidisciplinary pharmacometric mindset in young scientists is the understanding of fundamental principles of pharmacokinetics, pharmacodynamics, biopharmaceutics and pathophysiology. Dedicated modules in these basic sciences could be part of international training programs and included as recommended or mandatory parts of graduate programs. What can be left for on-the-job training might differ for students from different scientific backgrounds. Furthermore, the required expertise will strongly depend on the area in which a pharmacometrician works. Therefore, to build a one-size-fits-all university educational program is challenging (e.g., clinical, preclinical, or authorities). Instead, education could focus on a curriculum based on a desired set of core competencies. Multidisciplinary and specialized (under-) graduate courses could be developed in consensus with the pharmacometrics community and recognized by a professional international body, which would help to attract interested students from various disciplines early



on. Our colleagues have provided more details about the practical implementation of such an approach from a US perspective.

The aforementioned multidisciplinary mind-set allows pharmacometricians to be "good model communicators" who can efficiently translate between different disciplines, and identify the most impactful question for pharmacometric analyses. ¹⁰ Therefore, training to communicate results, implications, and assumptions of pharmacometric analyses should be considered equally important as methodological training. Good model communicators are pivotal for a sustainable future of pharmacometrics and to facilitate the move from an expert discipline to a fully embedded discipline within project teams.

Challenges and opportunities related to the unbalanced spread of pharmacometrics

The pharmacometrics community is relatively small but globally spread. A combination of local, international, and global collaborations could lead to optimal use of the unique insights across the world and allow students access to a large international network. International organizations such as the International Society of Pharmacometrics and WCoP are facilitating and spearheading global networking and collaboration initiatives. Furthermore, in past years, hybrid and remote working formats have been shown feasible for a pharmacometrics career. Especially smaller research groups and consulting companies have taken the opportunity to recruit from anywhere on the globe while allowing pharmacometric talents to work in their original country. This might improve talent retention and also allow better collaboration between remote-working pharmacometricians and local academic groups to foster local development of pharmacometric groups and strengthen the connection in the pharmacometrics community.

ROADMAP FOR NEXT STEPS

Training the next generation of pharmacometricians is a challenging task. Until now, it has been tackled through varying approaches across the globe, showcasing unique local challenges that might (only) be solved on a global scale. For example, the practical implementation of such an approach from a US perspective is provided in a companion paper to this one (under review). Indeed, joint efforts for continuous and sustainable development of pharmacometrics are crucial: overarching umbrella initiatives, for example, led by one of the hosts of the large pharmacometrics meetings, such as PAGE, ACoP, or WCoP, connect local initiatives such as the networks and training programs here (RedIF, PMXAfrica,

PharMetrX) and others (Asian Pharmacometrics Network. PAGANZ) and share their strengths while mitigating their challenges and weaknesses. This could lead to a centralized location where interested students can learn about pharmacometrics and which training opportunities exist within reach, i.e. an expansion of the ISoP website with all pharmacometric training programs and networks could be a good starting point. Stronger collaboration between academia and the pharmaceutical industry in the form of internships, scholarships, and exchanges could foster the sustainable growth of pharmacometric skills in early career scientists across the globe. Furthermore, financial and mentoring support also of the pharmaceutical industry of pharmacometricians-in-training in the form of scholarships, academic-industry exchanges and sponsored conference attendance could, especially in LMIC, increase the retention of these young talents locally. As a next step, an open debate across the pharmacometrics community on how to tackle the identified challenges would be beneficial. We invite the readers and the global pharmacometrics community to reach out with their point of view, ideas, or suggestions in an open debate to achieve this goal.

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CONFLICT OF INTEREST STATEMENT

The authors declared no competing interests for this work.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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